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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/993,366	11/21/2001	George Jackowski	2132.101	5753

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EXAMINER	
DAVIS, DEBORAH A	

ART UNIT	PAPER NUMBER
1641	17

DATE MAILED: 12/03/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/993,366	JACKOWSKI ET AL.	
	Examiner	Art Unit	
	Deborah A Davis	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *16 September 2003* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1 and 39-46* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1 and 39-46* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

1. Applicant's response to the Office Action mailed September 16, 2003 (Paper #11) is acknowledged. Currently, claims 1, 39-46, which includes SEQ ID NO. 1 are under consideration.

Claim Rejections - 35 USC § 112

2. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

3. Claims 1, 39-46 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Applicant has amended claims 1, 39-46 to include a biopolymer marker peptide consisting of amino acid residues 2-12 of SEQ ID NO:1, there is no support in the specification. Applicant is invited to show support or cancel new matter.

Claim Rejections - 35 USC § 112

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 1, 39-46 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. The claims are directed to a biopolymer marker peptide consisting of SEQ ID NO:1 diagnostic for insulin resistance, methods of using and a kit. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention.

Enablement requires that the specification teach those in the art to make and/ or use the invention without undue experimentation. Factor to be considered in determining, whether a disclosure would require undue experimentation include 1) the nature of the invention, 2) the state of the prior art, 3) the predictability or lack thereof in the art, 4) the amount of direction or guidance present, 5) the presence or absence of working examples, 6) the quantity of experimentation necessary, 7) the relative skill of those in the art, and 8) the breadth of the claims.

The nature of the invention – the invention is directed to a biopolymer marker peptide for insulin resistance, method and kit of using said marker consisting of SEQ ID NO:1.

The state of the prior art – the prior art of record fails to disclose a biopolymer marker peptide for insulin resistance, method and kit consisting of SEQ ID NO:1.

The predictability or lack thereof in the art – there is no predictability based on the instant specification that the protocol for isolating SEQ ID NO:1 is diagnostic of

insulin resistance. The instant specification fails to correlate (pages 40-46) SEQ ID NO's 1 to insulin resistance.

The amount of direction or guidance present – The specification fails to provide any clear guidance in Figure 1 distinguishing insulin resistance as a marker to the presence of the marker in healthy patients. In other words, there is the presence of the marker in healthy patients and also the presence of the marker in one patient with insulin resistance and absent in the other patient with insulin resistance (see Figure 1).

The presence or absence of working examples – Figure 1 is provided in the specification as a working example, however SEQ ID NO's 1 is not correlated to the marker for insulin resistance.

The quantity of experimentation necessary – it would require undue amount of experimentation for the skilled artisan to use the method as claimed.

The relative skill of those in the art – the level of skill in the art is high.

The breadth of the claims – as recited, the instant claims are directed to a biopolymer marker peptide for insulin resistance consisting of SEQ ID NO: 1. The claims are also directed to a method and kit consisting of SEQ ID NO: 1.

While the specification gives examples of protocols and recites that SEQ ID: NO's 1 would be the end result (page 46) it is unclear as to how this peptide correlate to insulin resistance because the data shown in Figure 1 is ambiguous.

Tockman et al. (Cancer Research 52 :27 :2711-2718, 1992) teach considerations necessary for a suspected cancer biomarker (intermediate end point marker) to have

efficacy and success in a clinical application. Although the reference is drawn to biomarkers for early lung cancer detection, the basic principles taught are clearly applicable to other **insulin biomarkers**. Tockman teaches that prior to the successful application of newly described markers, research must validate the markers against acknowledged disease end points, established quantitative criteria for marker presence/absence and confirm marker predictive value in prospective population trials, see abstract. Early stage markers of carcinogenesis have clear biological plausibility as markers of pre-clinical cancer and **if validated,** can be used for population screening (page 2714, column 1). The reference further teaches that once selected, the sensitivity and specificity of the biomarker must be validated to a known (histology/cytology-confirmed) cancer outcome. The essential element of the validation of an early detection marker is the ability to test the marker on clinical material obtained from subjects monitored in advance of clinical cancer and link those marker results with subsequent histological conformation of disease. "This irrefutable link between antecedent marker and subsequent acknowledged disease is the essence of a valid intermediate end point [marker]" (see page 2714, column 1) Biomarker Validation against Acknwledged Disease End Points section. Clearly, prior to the successful application of newly described markers, markers must be validated against acknowledged disease end points and the marker predictive value must be confirmed in prospective population trials, see page 2716, column 2, Summary section. Tockman reiterates that the predictability of the art in regards to cancer prognosis and the

estimation of life expectancies with a population with a disease or disorder is highly speculative and unpredictable.

Therefore, in view of the insufficient guidance in the specification, it is maintained that one of ordinary skill in the art could not use the invention as claimed without undue experimentation.

Response to Arguments

6. Applicant's arguments filed September 16, 2003 have been fully considered but they are not persuasive.

7. In response to Applicant's argument requesting for clarification of restriction requirement, see status of claims above.

8. Applicant's argument that the instant specification teaches those of skilled in the art how the claimed peptides were isolated and identified is acknowledged. However, Applicant has not show how to use SEQ ID NO 1. The specification does not enable one of ordinary skill in the art to correlate SEQ ID NO. 1 with insulin resistance. The drawings does not correlate SEQ ID NO. 1 to insulin resistance. In other words it is not clear what band, if any correlates to SEQ ID NO. I. Further the data presented in Figure 1 is ambiguous. For example, band 7 is seen in one insulin resistant patient but not in the other insulin resistant patient. In band 6, a marker seem to show up in Diabetes Type II and insulin resistance. Since data is amgiguous and confusing, it is hard to ascertain a substantial and credible use. Enablement requires that the specification

should teach how to make and use. Although one of ordinary skill in the art can isolate a peptide, applicant has not shown how this peptide correlates to SEQ ID NO 1 for insulin resistance.

9. Applicant's argument that the peptide consisting of amino acid residues 2-12 of SEQ ID NO. 1 was identified from protein fragments present in band 7 as a fragment of apolipoprotine A-IV precursor protein is not found persuasive because there is not support in the specification.

10. Applicant's argument that Figure 1 indicate that samples where taken from 5 patients that exhibited disease states and compared with samples from healthy patients is not found persuasive because there is no support in specification. On page 31 of the specification, applicant asserts that samples may be taken from a patient at one point in time, as a single sample or as multiple samples or at different points in time such that analysis is carried out on multiple samples for ongoing analysis. The specification further recites that a sample is taken from a patient that may have possible symptoms of a disease and is analyzed. After 3-6 months from the first sample taken, another one may be taken and analyzed to diagnose or monitor a disease state and Figure 1 does not explain the data.

11. Applicant argues that the Tockman et al reference and the instant invention are both drawn to identifying biomarkers, but not considered analogous since a direct

parallel can not be drawn between the neoplastic disease process and the process of insulin resistance is not found persuasive. The Tockman et al reference and the instant application are analogous because both are drawn to biopolymer research indicative of a disease state. Although Tockman et al was published 10 years ago, it still holds true that extensive experimentation is required to determine biopolymers markers and the specification has not shown clear validation of this data.

12. The declaration under 37 CFR 1.132 filed September 16, 2003 is insufficient to overcome the rejection of claims 1, 39-46 based upon 112 first rejection as set forth in the last Office action because: Applicant's declaration was not found persuasive because the data in Figure 1 is ambiguous. The normal patient exhibited a strong presence of the marker while the other two normal patients exhibited a weak presence of the marker. The diseased patient exhibited also a weak presence for insulin resistance making it hard to distinguish if the biomarker is indicative of insulin resistance. Therefore, rejection is maintained and made final.

Conclusion

13. No claims are allowed.

14. THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Deborah A Davis whose telephone number is (703) 308-4427. The examiner can normally be reached on 8-5 Monday thru Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le can be reached on (703) 305-3399. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-1123.

Deborah A. Davis
CM1, 7D16
November 21, 2003

LONG V. LE
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600
11/25/03